

Hair Regeneration-Mesenchymal Stem Cell

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INTRODUCTION

Hair loss is a quite common condition observed in both men and women. Pattern hair loss also known as androgenetic alopecia is the most common form of hair loss that is thought to affect up to 80% of Caucasian men and up to 40% of Caucasian women by age of 70, and it can have quite devastating consequences on one's well-being, including lower self-esteem, depression and lower quality of life.

In the past decade, hair regeneration research has plummeted, including the discoveries regarding stem-cell based therapies leading to many preclinical and some clinical studies with encouraging outcomes. Stem-cell transplant, stem cell-derived Conditioned Medium (CM) and stem cell-derived exosomes have recently gained a lot of attention as potential new agents to modify and enhance the signaling pathways that could induce HFSC reactivation, hair cycle and hair follicle regeneration. In this review, we will provide resources to the preclinical studies, but our major focus will be on the latest clinical research as it relates to stem-cell based therapies, hair loss, and hair regeneration potential.

Alopecia is characterized by hair loss in one or more regions of scalp or body. The prevalence rate is 2.1% in USA with global incidence risk rate of 2%. Several factors including stress, hereditary, nutritional disorders, and thyroid functional abnormalities, psychological, genetic, and immune disorders have been held responsible for triggering of disease. Though, the disease is not life threatening, it is associated with aesthetic values and self-dignity. The commencement of disease in early age can cause psychological concerns like low self-esteem, depression, or anxiety, affecting the quality of life. Alopecia Areata (AA), specifically, is an autoimmune disorder caused due to targeting of immune-privileged Hair Follicles (HF) by T cells.

To date there have only been 2 FDA approved medications, minoxidil and finasteride, but their effects are often unsatisfactory and temporary, in addition to having various adverse effects. Stem cell-based therapies have recently received lots of attention as potential novel treatments that focus on reactivating hair follicle stem cells and in this way enhance hair

follicle growth, regeneration and development. Stem cell-based therapy approaches include stem cell transplant, stem cell-derived conditioned medium and stem cell-derived exosomes.

AA is characterized by patchy scalp hair loss which may progress to complete scalp hair loss (alopecia totalis) or complete body hair loss (alopecia universalis). The incidence of AA is associated with co-occurrence of other autoimmune disorders like psoriasis, vitiligo, systemic lupus erythematosus, rheumatoid arthritis, and inflammatory bowel disease. Further, thyroid related abnormalities are frequently found in AA patients. Diabetes mellitus co-occurrence with AA has been reported in patients with increased insulin resistance.

The current available interventions include topical minoxidil, topical anthralin, intralesional corticosteroids injections; topical corticosteroids contact sensitizers, and Psoralen plus Ultraviolet an Irradiation (PUVA) therapy. These therapeutic approaches are either partially successful or are associated with significant side effects. HF transplant is mediated by advanced surgical procedures involving implantation of hair follicles to region without hair. The success of procedure is limited due to poor availability of donors, low survival of transplants, painful procedures, and expensive treatment.

PHL is a form of non-scarring alopecia. PHL is characterized by defects in and loss of hair progenitor cells, while Hair Follicle Stem Cells (HFSCs) remain viable. This notion in particular makes PHL a reversible condition and current and novel treatment modalities attempt to utilize the existent viability and responsiveness of HFSCs as to reverse hair loss pathology and promote hair growth. Providing adequate signals and environment to reactivate HFSCs and regrow a hair follicle is of particular interest to the hair regeneration scientific and clinical community.

Further, the results achieved are often temporary. Strategies based on stem cells are under investigation for their ability to regenerate the lost hair follicle and stimulate hair growth. Mesenchymal Stem Cells (MSCs) particularly have drawn attention of researchers and clinicians owing to ease of availability, immune-privileged nature and regenerative capacity. MSCs are multipotent cells present in multiple tissues including

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adipose, umbilical cord, bone marrow, hair follicle, dental pulp and liver. These are characterized by high proliferative capacity, plastic adherence, and spindle shape morphology. Some studies have demonstrated the therapeutic efficacy MSCs in HF regeneration. However, the regenerative potential of MSCs has been attributed to the growth factors they secrete.

Though, pre-clinical and clinical studies have investigated effect of MSC-CM on hair growth and demonstrated its positive effect; mainly intradermal injections were used, which is invasive in nature used micro needle roller prior to topical application of conditioned medium of adipose tissue derived stem cells. Frequent usage of intradermal injections is challenging for

patients as it requires regular clinic visits, cause pricking discomfort, and impose fear of infection. This report highlights simple approach of topical application of MSC-CM for alopecia patients in self applicable mode without distress and possibility of infection. The microfiltration procedure used to filter MSC-CM make peptides size even, remove aggregates and improves diffusibility across the scalp. Further, MSC-CM contains lipid bound exosomes which are enriched in growth related proteins, DNA and RNA. These exosomes can integrate with lipid membrane of hair scalp cells and facilitate the transfer of liposomal materials.